We claim:

1. A Y-shaped branched hydrophilic polymer derivative represented by formula I:

$$P_a \text{----} X_1$$
$$P_b \text{----} X_2 \diagdown N \text{---} (CHR_i)_j \text{------} F \qquad (I)$$

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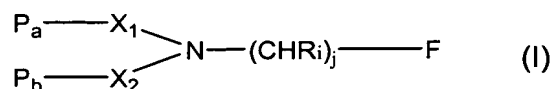
wherein

P_a and P_b are hydrophilic polymers, which are the same or different;

j is an integer from 1 to 12;

R_i is selected from the group consisting of H, a C_{1-12} substituted or unsubstituted

10   alkyl, a substituted aryl, an aralkyl, and a heteroalkyl;
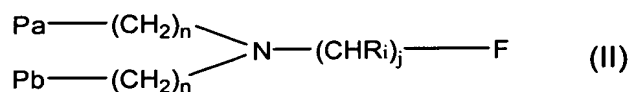
X_1 and X_2 independently are linking groups, wherein X_1 is $(CH_2)_n$, and X_2 is

selected from the group consisting of $(CH_2)_n$, $(CH_2)_nOCO$, $(CH_2)_nNHCO$ and

$(CH_2)_nCO$, wherein n is an integer of from 1-10; and

F is a functional group selected from the group consisting of a hydroxyl group, a

15   carboxyl group, an ester group, carboxylic acid chloride, hydrazide, maleimide

and pyridine disulfide, being capable of reacting with an amino group, a

hydroxyl group or a thiol group of a therapeutic agent or a substrate to form a

covalent linkage.

2. The hydrophilic polymer derivative of claim 1 wherein the hydrophilic

20   polymer is selected from the group consisting of polyethylene glycol, polypropylene

glycol, polyvinyl alcohol, polyacrylmorpholine and copolymers thereof.

3. The hydrophilic polymer derivative of claim 2 wherein the hydrophilic

polymer is polyethylene glycol.

4. A Y-shaped branched polyethylene glycol derivative represented by formula

25   II:

$$Pa\text{------}(CH_2)_n$$
$$\begin{array}{c} \searrow \\ N\text{---}(CHR_i)_j\text{------}F \\ \nearrow \end{array} \quad \text{(II)}$$
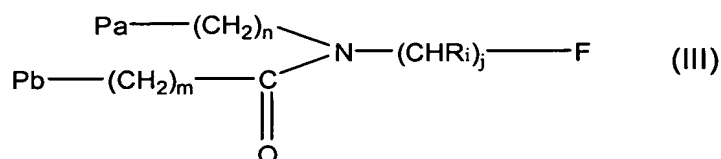$$Pb\text{------}(CH_2)_n$$

wherein

P_a and P_b are polyethylene glycols, which are the same or different;

n and j are independently an integer from 1 to 12;

5   R_i is selected from the group consisting of H, a C_{1-12} substituted or unsubstituted

alkyl, a substituted aryl, an aralkyl, and a heteroalkyl; and

F is a functional group selected from the group consisting of a hydroxyl group, a

carboxyl group, an ester group, carboxylic acid chloride, hydrazide, maleimide

and pyridine disulfide, being capable of reacting with an amino group, a

10   hydroxyl group or a thiol group of a therapeutic agent or a substrate to form a

covalent linkage.

5. A Y-shaped branched polyethylene glycol derivative represented by formula

III:

$$Pa\text{------}(CH_2)_n$$
$$\begin{array}{c} \searrow \\ N\text{---}(CHR_i)_j\text{------}F \\ \nearrow \end{array} \quad \text{(III)}$$
$$Pb\text{------}(CH_2)_m\text{------}\underset{\underset{O}{\parallel}}{C}$$

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wherein

P_a and P_b are polyethylene glycols, which are the same or different;
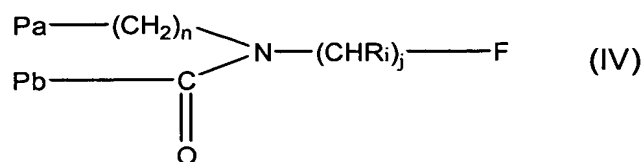
n, m and j are independently an integer from 1 to 12;

R_i is selected from the group consisting of H, a C_{1-12} substituted or unsubstituted

20   alkyl, a substituted aryl, an aralkyl, and a heteroalkyl; and

F is a functional group selected from the group consisting of a hydroxyl group, a

carboxyl group, an ester group, carboxylic acid chloride, hydrazide, maleimide

and pyridine disulfide, being capable of reacting with an amino group, a

hydroxyl group or a thiol group of a therapeutic agent or a substrate to form a

covalent linkage.

6. A Y-shaped branched polyethylene glycol derivative represented by formula IV:

$$Pa \text{---} (CH_2)_n \diagdown$$
$$\qquad\qquad\qquad\qquad \diagdown N \text{---} (CHR_i)_j \text{-----} F \qquad (IV)$$
$$Pb \text{-----} \underset{\substack{\| \\ O}}{C} \diagup$$
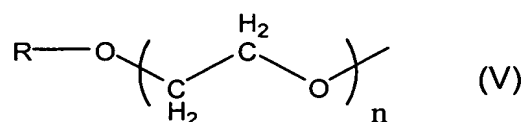
5   wherein

P_a and P_b are polyethylene glycols, which are the same or different;

n and j are independently an integer from 1 to 12;

R_i is selected from the group consisting of H, a C_{1-12} substituted or unsubstituted

alkyl, a substituted aryl, an aralkyl, and a heteroalkyl; and

10   F is a functional group selected from the group consisting of a hydroxyl group, a

carboxyl group, an ester group, carboxylic acid chloride, hydrazide, maleimide

and pyridine disulfide, being capable of reacting with an amino group, a

hydroxyl group or a thiol group of a therapeutic agent or a substrate to form a

covalent linkage.

15   7. The derivative of any one of claims 1 to 6, wherein P_a and P_b are the same or

different PEGs of formula (V):

$$R \text{-----} O \diagup\kern-0.5em\diagup \underset{H_2}{C} \diagdown \overset{H_2}{\underset{}{C}} \diagdown O \diagup\kern-0.5em\diagup_n \qquad (V)$$

wherein

R is H, a C_{1-12} alkyl, a cycloalkyl or an aralkyl; and

20   n is an integer, representing the degree of polymerization.

8. The derivative of claim 7, wherein R is selected from the group consisting of

H, methyl, ethyl, isopropyl, cyclopropyl, cyclobutyl, cyclohexyl and benzyl.

9. The derivative of claim 7, wherein the molecular weight of PEG is from

about 300 to 60000.

10. A method to prepare the PEG derivative of claim 4, comprising :

at 0 ℃ initiating the polymerization of ethylene oxide with N,N-di-2-hydroxylethyl- 2-benzyloxyethyl amine in the presence of a catalyst;

alkylating terminal hydroxyl groups;

removing benzyl groups by catalytic hydrogenation; and

derivatizing the new hydroxyl group to incorporate the terminal group F..

11. A method to prepare the PEG derivative of claim 5 or 6, comprising:

reacting one methoxyl polyethylene glycol mesylate with an amino acid under basic conditions to produce a reactive product; and

reacting the reactive product obtained above with another methoxyl polyethylene glycol derivative, and further derivatizing to incorporate a terminal group F.

12. The method of claim 11, wherein the another methoxyl polyethylene glycol derivative is mPEG-carboxyethyl NHS ester.

13. A conjugate formed by reacting the derivative of any one of claims 1, 4, 5 and 6 with drug molecules through the terminal group F.

14. A copolymer of the derivatives of any one of claim 1, 4, 5 and 6 and other polymers linked through the terminal group F.

15. The conjugate of claim 13 wherein the drug is selected from the group consisting of amino acids, proteins, enzymes, nucleosides, saccharides, organic acids, glycosides, flavonoids, anthraquinones, terpenoids, phenylpropanoid phenols, steroids, glycoside of the steroids and alkaloids of the steroids.

16. The conjugate of claim 13 wherein the drug is an active component of a natural medicine.

17. The conjugate of claim 16 wherein the active component is cinobufagin,

clycyrrhetinic acid or scopoletin.

18. The conjugate of claim 13 wherein the drug is an anti-tumor agent.

19. The conjugate of claim 18 wherein the anti-tumor agent is selected from the group consisting of paclitaxel, camptothecin, interferon and derivatives thereof.

5   20. The conjugate of claim 19 wherein the interferon is α-, β-or γ-interferon.

21. A pharmaceutical composition comprising the conjugate according to any one of claims 13 to 20 and optionally a pharmaceutically acceptable carrier and excipient.

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